REMARKS

In the Office Action dated July 10, 2009, claims 1-3, 5, 9-33, 36-38, 41-44, 60-63 and 66-70 were indicated as pending in the application, with claims 16-32, 60-63 and 66-70 indicated as being withdrawn. The Examiner should note that claim 65 was pending (although withdrawn), and is still pending.

Applicants have now cancelled claims 60-62, amended claims 1, 2, 11 and 67-69, and (consistent with Applicants' prior listing), claims 16-32, 63, 65 and 66 remain withdrawn. New claims 71-74 have been added. Care has been taken to avoid the introduction of new matter. Thus, claims 1-3, 5, 9-15, 33, 36-38, 41-44 and 67-74 are presently pending and presented for examination.

In the Office Action the Examiner has indicated his belief that claims 67-70 are directed to an invention that is independent and distinct from the invention originally claimed. The Office Action states: "[t]he new claims are related to the claims already examined as combination/subcombination . . . In the instant case, the combination as claimed does not require the particulars of the subcombination as claimed for patentability because even if the subcombination is unpatentable, the combination of the subcomponent bound to a surface might be patentable." Accordingly, independent claim 67 has been amended to remove the limitation that the copolymer is bound to a surface. For this reason, Applicants submit that claims 67-70 should not be withdrawn.

Claim Amendments

Claim 1 and claim 67 have been amended to indicate that c1) is a primary amine group. This amendment is supported by, for example, page 17, lines 10-11. Claim 1 and claim 67 have also been amended to indicate that the structure of the claimed copolymer permits binding the copolymer-linked bifunctional reagent to the surface modifying substance d) without substantial loss of bioactivity of such substance in an instant reaction at room temperature with a solution or suspension comprising the surface-modifying substance d). This amendment is supported by the specification at, for example, page 19, lines 1, 2 and 28-30 and page 20, lines 1-10 and 15-21.

New claims 71 and 72 are drawn to a preferred embodiment of the invention. Claim 71 is drawn to a block co-polymer in which a) comprises a PLA, c1) comprises a hydroxyl group, b) comprises polyethylene glycol, c) c2 comprises a primary amine, and in which the bifunctional reagent is selected from disuccinimidyl tartaric acid and disuccinimidyl succinate. Support for this amendment can be found, for example, at page 16, lines 10-21 and 26-29; page 17, lines 4-10; page 18, lines 23-25; and page 24, lines 6-8.

Claim 72 is drawn to the block co-polymer of claim 71 in which the hydrophobic block has a molecular weight of 100-100,000 Da and the hydrophilic block contains a PEG-NH_2 moiety having a molecular weight of up to about 10,000 Da. Support for this claim can be found, for example, at pages 16 and 17 of the specification.

Claim 73 is drawn to the block co-polymer of claim 71 having a specific formula, wherein a) is a polylactate and b) is a polyethylene glycol, c1) is O and c2 is NH_2, and wherein the minimum number of lactide residues is about 19 (molecular weight 1,000 Da) and the

minimum number of ethylene glycol residues is about 5 (molecular weight 200 Da). Claim 74 is drawn to the block co-polymer of claim 71 wherein the maximum molecular weight of the polylactide moiety and the PEG moiety, respectively, is about 100,000 Da and about 10,000 Da. Support for these amendments can be found in the specification at, for example, pages 16 and 17.

Rejection pursuant to 35 U.S.C. §102(e)

Claims 1-3, 5, 11, 14, 15 and 33 were again rejected as allegedly being anticipated pursuant to 35 U.S.C. §102(e) over Hirosue et al. (US 6254890). Independent claim 1 has now been amended to indicate that c1) is a primary amine group and that the structure of the claimed copolymer permits binding the copolymer-linked bifunctional reagent to the surface modifying substance d) without substantial loss of bioactivity of such substance in an instant reaction at room temperature with a solution or suspension comprising the surface-modifying substance d). To the extent that this rejection is maintained against the claims as presently amended, Applicants traverse this rejection for the following reasons.

A patent claim is not anticipated pursuant to 35 U.S.C. §102 unless a single prior-art reference contains each and every limitation of the claim, adequately describes the invention, and teaches a person of skill in the art to make and use the invention without undue experimentation. *See e.g., In re Paulsen*, 30 F.3d 1475, 31 USPQ 2d 1671 (Fed. Cir 1994).

Applicants hereby incorporate by reference, *mutatis mutandis*, the arguments made in responses to previous Office Actions traversing the 35 U.S.C. §102 rejections. By amending the claims, Applicants in no way concede the contention that the previous claims were drawn to an invention that had been previously described, known, or used by Hirosue et al. or was otherwise

unpatentable. However, in the interests of obtaining the allowance of claims directed to the preferred embodiments of the invention, Applicants have amended claim 1 to contain further limitations that are nowhere disclosed or even suggested by Hirosue et al.

Thus, the present claims are drawn in part to a copolymer comprising a hydrophobic group selected from one or more of polylactide, polyglycolide, poly(lactide-co-glycolide), poly-β-hydroxybutyrate and poly-β-hydroxyvalerate, a hydrophilic polymer comprising polyethylene glycol, and a linking group comprising a primary amine, wherein the structure of the copolymer permits binding the copolymer-linked bifunctional reagent to the surface modifying substance d) without substantial loss of bioactivity of such substance in an instant reaction at room temperature with a solution or suspension comprising the surface-modifying substance d).

The previous Office Actions have depended upon Example 4 of the '890 patent to make their case alleging lack of novelty. However, Example 4 states in full:

> Method for Attaching Surface-Masking and/or Targeting Moieties
>
> Surface masking characteristics are provided by PEG on the nanospheres by using various PEG-PLA and PLGA mixtures in the initial polymer solution. Non-covalent attachment of targeting moieties is achieved by incubating biotin-PEG-PLA: PLGA nanospheres with excess streptavidin or avidin, in turn, incubating the avidinylated spheres with biotin-ligand. **Covalent attachment methods use activated esters (N-hydroxysuccinimidyl esters) on PEG-PLA with which amine groups from desirable ligands can be reacted.**

The Office Action supports the novelty rejection by contending, in response to the fact that Hirosue et al. does not actually mention poly(ethylene glycol) amine (a feature of the pending claims), that Hirosue et al. actually does implicitly teach amine terminated PEG because "[w]hen Ny-hydroxysuccinamide is attached to the terminus of PEG, it is by way of the nitrogen atom and the PEG terminus is in the form of an amine. Thus, Hirosue et al. implicitly teaches amine terminated PEG."

Leaving aside for the moment the fact that Example 4 provides no description at all on how to make or use the present invention, the argument quoted above is circular in that it assumes without any support that PEG is terminated with an amine, which is exactly the thing that it purports to prove. Applicants respectfully ask the Examiner to point out the evidence on Hirosue et al. demonstrating that when Ny-hydroxysuccinamide is attached to the terminus of PEG, it is by way of a nitrogen atom. Applicants note that PEG contains no nitrogen atom.

Claims 73 and 74 are drawn to specific embodiments of the present invention, within a specific molecular weight range. Hirosue et al. neither discloses nor suggests such compounds.

Since the Office Action neither cites nor provides any basis for the contention that Hirosue et al. either explicitly or implicitly discloses all of the limitations of claims 1-3, 5, 11, 14, 15 and 33, particularly in light of the present amendments, this rejection is believed to be overcome.

Rejection of claims 1-3, 5, 9-15, 33, 36-38 and 41-44 under 35 U.S.C. §103(a)

Similarly, claims 1-3, 5, 9-15, 33, 36-38 and 41-44 were rejected as allegedly being obvious over Hirosue et al. in view of Domb et al. Applicants respectfully traverse this

rejection for the reasons provided above, and for the additional reasons given below. Additionally, Applicants incorporate by reference, *mutatis mutandis*, the arguments made in responses to the previous Office Actions concerning non-obviousness of those claims into the context of the present claims.

As stated above, Hirosue et al. does not disclose the present invention. Moreover, noting that the disclosure of that reference's teaching and/or combination is insufficient to encompass the content of same claims as a whole, Domb et al., when combined with Hirosue et al., still does not fill-in for or make-up for the deficiencies of Hirosue et al. Since the content of a combination of elements cannot be more than the parts making up that combination, even if there were some teaching or suggestion to combine Hirosue et al. with Domb et al., all of the elements of, for example, each of the independent claims, still would not be met.

Moreover, as an example, Hirosue et al. in no way discloses, teaches, or even suggests a linear block copolymer, comprising the structure c2)-b)-c1)-a), wherein:

- a), the hydrophobic polymer, is selected from one or more of polylactide, polyglycolide, poly(lactide-co-glycolide), poly-β-hydroxybutyrate and poly-β-hydroxyvalerate,
- c1) comprises a hydroxyl group,
- b) comprises a PEG, and
- c2) comprises a primary amine able to bind a bifunctional reagent such that the structure of the copolymer permits binding the copolymer-linked bifunctional reagent to the surface modifying substance d) without substantial loss of bioactivity of such substance in an instant reaction at room temperature with a solution or suspension comprising the surface-modifying substance d).

As discussed in prior responses, Hirosue et al. is not prior art against any of the present claims pursuant to e.g., *Alexander Milburn Co. v. Davis-Bournonville Co.,* 270 U.S. 390 (1926)(hereinafter *Milburn*), and *In re Wertheim and Mishkin*, 209 USPQ 554 (CCPA 1981)(hereinafter *Wertheim*). However, even assuming, *arguendo,* that Hirosue is prior art, it does not render the present invention obvious, either alone or in combination with Domb et al. Hirosue et al. does not discuss or even suggest linear polymers of modified PEGs, as are claimed in the pending claims.

Claims 73 and 74 are drawn to specific embodiments of the present invention, within a specific molecular weight range. Hirosue et al. (and Hirosue et al. and Domb et al.) neither discloses nor suggests such compounds; Domb et al. is cited solely for providing the molecular weights of PEG-PLA polymers. Hirosue et al. and Domb et al., if combined, completely fail to suggest all of the limitations of the present claims, and thus to render the present invention obvious.

Additionally, as further evidence of the non-obviousness of the present invention, Applicants herein enclose three scientific papers, published after the filing date of the present application by one or more of the inventors. These papers clearly indicate that even as late as 2004 (about 4 years after the July 5, 2000 §371(c) priority date of the present patent application), the claimed invention was regarded as new and innovative in its ability to rapidly create new biomimetic surfaces without causing inactivation of the surface-modifying substances, and without the need to derivatize the substances prior to binding them. *See* Tessmar, Joerg K., Miko, Antonio G., and Gopferich, Achim, *Amine-Reactive Biodegradable Diblock Copolymers*, 3: BIOMACROMOLECULES 194-200 (2002); Tessmar, Joerg, Miko, Antonio, and Gopferich, Achim, *The Use Of Poly(ethylene glycol)*-Block-*Poly(lactic Acid) Derived Copolymers For The Rapid Creation Of Biomimetic Surfaces*, BIOMATERIALS 24:4475-4486 (2003); Tessmar et al.,

Towards The Development Of Biomimetic Polymers By Protein Immobilization: PEGylation Of Insulin As A Model Reaction, TISSUE ENGINEERING 10:441 (2004).

According to MPEP 2143.03, if an independent claim is nonobvious under 35 U.S.C. §103, then any claim depending therefrom is nonobvious. In re Fine, 837 F.2d 1071, 5 USPQ2d 1596 (Fed. Cir. 1988). It is submitted that each of the presently pending dependent claims is allowable at least because of the dependency upon its corresponding independent base claim, and further because of the additional limitations recited therein. Thus, all of the pending dependent claims are believed also to be allowable.

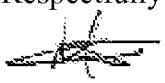
The rejections present no viable evidence sufficient to show a lack of novelty or to show that one with ordinary skill in the art would have considered the claimed invention to have been obvious through the disclosures and teaching of Hirosue et al. in view of Domb et al. According to the above amendments and arguments, the rejections have presented no evidence to show that anticipation or a prima facie case of obviousness can be established. Accordingly, Applicants respectfully submit that the claimed invention is allowable over each of Hirosue et al. and Domb et al.

Conclusion

For the reasons presented above, Applicants submit that the claims are in condition for allowance, and request reconsideration and withdrawal of the rejections under 35 U.S.C. §102 and §103. In view of the above, the Examiner is requested to consider the application now to be in condition for allowance, and an early indication of same is requested. The Examiner is invited to contact the undersigned with any questions.

The Commissioner is hereby authorized to charge any needed fees to Deposit Account 50-1600.

Respectfully submitted,



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